



## PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT  
(PCT Article 36 and Rule 70)10/522389  
REC'D 24 SEP 2004WIPRO PCT  
25 JAN 2005

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|--|--|---|--|
| Applicant's or agent's file reference<br>N.84450A SMW  |  | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)  |  |
| International application No.<br>PCT/EP 03/08216   | International filing date (day/month/year)<br>25.07.2003 | Priority date (day/month/year)<br>25.07.2002  |  |
| International Patent Classification (IPC) or both national classification and IPC<br>C12N9/00  |  |   |  |
| Applicant<br>DSM IP ASSETS B.V. et al.   |  |   |  |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>  |  |   |  |
| <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"><li>I <input checked="" type="checkbox"/> Basis of the opinion</li><li>II <input type="checkbox"/> Priority</li><li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li><li>IV <input checked="" type="checkbox"/> Lack of unity of invention</li><li>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li><li>VI <input type="checkbox"/> Certain documents cited</li><li>VII <input type="checkbox"/> Certain defects in the international application</li><li>VIII <input type="checkbox"/> Certain observations on the international application</li></ul> |  |   |  |
| Date of submission of the demand<br><br>20.02.2004   |  | Date of completion of this report<br><br>23.09.2004   |  |
| Name and mailing address of the International preliminary examining authority:<br><br> European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465  |  | Authorized Officer<br><br>Kalsner, I<br><br>Telephone No. +49 89 2399-8708<br><br> |  |

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP 03/08216

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-63 as originally filed

**Claims, Numbers**

1-28 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.  
☒ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

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## IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

- ☒ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☒ the parts relating to claims Nos. 1-16, 27, 28, all partially; 23, 24, completely .

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

|                               |             |                      |
|-------------------------------|-------------|----------------------|
| Novelty (N)                   | Yes: Claims | 4, 5, 23, 24         |
|                               | No: Claims  | 1-3, 6-16, 27, 28    |
| Inventive step (IS)           | Yes: Claims |                      |
|                               | No: Claims  | 1-16, 23, 24, 27, 28 |
| Industrial applicability (IA) | Yes: Claims | 1-16, 23, 24, 27, 28 |
|                               | No: Claims  |                      |

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/08216

**Ad Section IV: Lack of unity of invention**

The International Preliminary Examining Authority (IPEA) is of the opinion that the present application does not comply with the requirement of unity as set forth in Art. 34(3) and Rule 13 PCT.

An international application must relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.

Unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same special technical features, special technical features being such features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The following four inventions have been identified:

**Invention 1: Claims 1-16, 27 and 28, partially:** a polypeptide, polynucleotide, vector, host cell, process of producing a polypeptide, and a process for producing vitamin B12 insofar as the subject-matter relates to SEQ ID NO: 1 and 2; **claims 17 and 18,** a process for the preparation of an amine

**Invention 2: Claims 1-16, 27 and 28, partially,** as above, but with respect to SEQ ID NO: 3 and 4; **claims 19-22,** processes for the preparation of a phosphate containing and a nucleotidyl-containing compound

**Invention 3: Claims 1-16, 27 and 28, partially,** as above, but with respect to SEQ ID NO: 5 and 6; **claims 23 and 24,** process for the preparation of an aryl-containing compound.

**Invention 4: Claims 1-16, 27 and 28, partially,** as above, but with respect to SEQ ID NO: 8 and 9; **claims 25, 26,** process for the preparation of an adenosine-containing compound

The technical relationship linking together the different sequences can be seen in the fact that they are coding for enzymes which are involved in the biosynthesis of vitamin B12.

Enzymes involved in the biosynthesis of vitamin B12, even from *Propionibacterium*

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EXAMINATION REPORT - SEPARATE SHEET**

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*freudenreichii*, are known in the state of the art (e.g. Roessner et al., 2002). This concept/relationship, therefore, cannot be accepted to constitute a special technical feature as defined above as it does not define a contribution which each of the different claimed inventions, considered as a whole, makes over the prior art.

Thus, the presently claimed subject-matter falls apart in the above groups of inventions which are not unitarian.

In their fax dated 5 April 2004 applicants requested to have invention 3 examined in the case examination will not extend to all four of the inventions identified in the international search report. Hence preliminary examination will be based on invention 3, i.e. the subject-matter identified above with respect to SEQ ID NO: 5 and 6.

**Ad Section V: Reasoned statement with regard to novelty, inventive step or industrial applicability**

- 1) The present application relates to nucleic acid sequences from *Propionibacterium freudenreichii* encoding enzymes involved in the biosynthesis of vitamin B12 and processes for the preparation of various compounds being intermediate products in the biosynthetic pathway of vitamin B12.

- 2) **Documents**

D1...Roessner et. al. (2002) Microbiol. 148: 1845-1853  
D2...WO-A-91 11518

- 3) **Novelty**

**Claims 1-3, 6-16, 27 and 28** are not considered to meet the requirements of Art. 33(2) PCT for the following reasons:

D1 discloses the isolation and characterisation of 14 genes from *P. freudenreichii* specifying the anaerobic biosynthesis of vitamin B12. Among the enzymes disclosed are synthases. D1 is therefore considered novelty destroying for claims 1, 2 and 16.

D2, too, discloses polypeptides involved in the biosynthesis of cobalamines and/or cobamides. The nucleic acids disclosed in D3 are derived from *Pseudomonas denitrificans*. The sequence of *cobS* shows 62% identity with SEQ ID NO: 5 of the present application. Furthermore, D3 discloses vectors and host cells containing *cobS* and processes of producing vitamin B12 (esp. claims 10, 11, 42, 46).

**Claims 1, 2, 6-19, 27 and 28** are thus not considered novel over D2.

**4) Inventive step**

Even if novelty could be established for the present claims an inventive step could not be acknowledged for the following reason:

D1 is considered to represent the closest prior art. D1 discloses most of the genes involved in the vitamin B12 biosynthesis. D1, however, states that the late-pathway genes *cobU*, *cobS* and *cobT* from *P. freudenreichii* have not yet been isolated.

The problem to be solved by the present application can thus be seen in the provision of *cobS* from *P. freudenreichii*.

*CobS* is known from other organisms, and has been characterised in D2 where it was derived from *P. denitrificans*. It thus is considered obvious for the skilled person to use the sequence information derivable from D2 in order to look for similar genes in *P. freudenreichii*.

**Claims 1-16, 23, 24, 27 and 28** are thus objected to under Art. 33(3) PCT.